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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/518,640

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Masayuki Furuya

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EXAMINER

KRISHNAN, GANAPATHY

ART UNIT

PAPER NUMBER

1623

NOTIFICATION DATE

DELIVERY MODE

03/10/2009

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ADIPFDD@bipc.com

Office Action Summary	Application No. 10/518,640	Applicant(s) FURUYA ET AL.	
	Examiner Ganapathy Krishnan	Art Unit 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 January 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 21-23 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 21-23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The amendment filed 1/14/2009 has been received, entered and carefully considered.

The following information provided in the amendment affects the instant application:

1. Claims 2-20 and 24-28 have been canceled.
2. Claim 1 has been amended.
3. Remarks drawn to rejections under 35 USC 103.

Claims 1 and 21-23 are pending in the case.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

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evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of Claims 1 and 21-23 under 35 U.S.C. 103(a) as being unpatentable over Toshiyuki et al (JP 62-263194, English translation; document listed in IDS of Aug. 23, 2005) in view of Yujiro et al (JP 2000-319116, English translation; listed in IDS of Aug. 23, 2005) both of record and March et al (General Organic & Biochemistry, 5th Ed., 1998, page 464) is being maintained for reasons of record reiterated below.

Toshiyuki et al teach a process of making a glycoside wherein pentaacetyl glucose (a sugar molecule having an acetyl group attached to the anomeric carbon) is reacted with hydroquinone (a dihydroxy phenol) in the presence of p-toluenesulfonic acid as catalyst in xylene, to give the corresponding glycoside (page 1, see below the sub heading-Prior art; page 3, paragraphs 8-10; comparative example 2, at page 5). Even though the term hydroquinone suggests that it is a ketone, the compound exists as a tautomer between a p-diketone and p-dihydroxy benzene, which is a phenolic compound with two hydroxyl groups. It reacts with pentaacetyl glucose via the dihydroxy tautomer to give the corresponding glycoside. The removal of acetic acid under vacuum (lower temperature) is suggested (page 3, paragraph 9). However, Toshiyuki et al do not teach the use of Lewis acid catalyst like boron trifluoride (even though tin tetrachloride is suggested) in their process.

Yujiro et al, drawn to gallic acid derivatives, teach the preparation of a glucoside derivative via the reaction of gallic acid (trihydroxy benzoic acid) or its ester (structure (2) in

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claim 11) with saccharide, including pentaacetyl glucose, that is completely acetylated, in the presence of Lewis acid catalyst, one of which is boron trifluoride etherate to give the corresponding glycoside (page 3, paragraph 0011; page 4, paragraph 0018). However, Yujiro et al do not exemplify their process using xylene as the solvent.

According to March et al a carboxylic acid like propionic acid (adjacent homolog of acetic acid produced in the instant method) reacts with a phenolic hydroxyl (reaction (b) as shown in March et al) in the presence of acid catalyst to give the corresponding ester. This means that this same type of esterification can also take place in the instant method between the acetic acid generated during the reaction of the first mole of glucose pentaacetate with the gallic acid ester with the monoglycoside formed in the first step to acetylate the phenolic OH. This is a side reaction that would prevent the formation of the diglycoside. In order to avoid this side reaction and facilitate the formation of the diglycoside as in instant claim 1 the acetic acid generated has to be removed from the reaction system. This will be recognized by one of ordinary skill in the art and hence one would remove the acetic acid from the system during the process.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the process as instantly claimed and taught by the prior art for making the glycoside as instantly claimed since the process for making such a glycoside using closely analogous starting materials, solvents and catalyst is taught in the prior art.

One of skill in the art would be motivated to use the method as instantly claimed, especially using boron trifluoride and xylene as solvent since the use of benzene as a solvent has a problem with temperature and pressure requirements for the removal of the acetic acid that is

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generated in the process and control of the reaction is difficult and yield is low (Toshiyuki: page 1, last paragraph though page 2, paragraph 2). Hence one of skill in the art would look for other closely related solvents and Lewis acid catalyst like boron trifluoride in order to have better control of the reaction, easy removal of acetic acid and also improve the yield. It is well within the skill of the artisan to adjust process conditions for the purpose of optimization and to use other derivatives of the phenolic compound as instantly claimed in claims 2-3, in order to extend the scope of the instant method.

Even though, Toshiyuki discloses (page 2, paragraph 3; page 5, comparative examples 2-3) that Wolfrom suggests xylene as solvent the yield is about 50%, one of skill in the art would be motivated to substitute other Lewis acid catalyst like boron trifluoride as suggested by Yujiro still using xylene as solvent in order to improve the yield since xylene has been successfully used as the reaction solvent. One of skill in the art would adjust the pressure and temperature for removal of the acetic acid that is formed in the process and thereby look for improvement in the yield of the desired product, with a reasonable expectation of success.

Response to Applicants Arguments

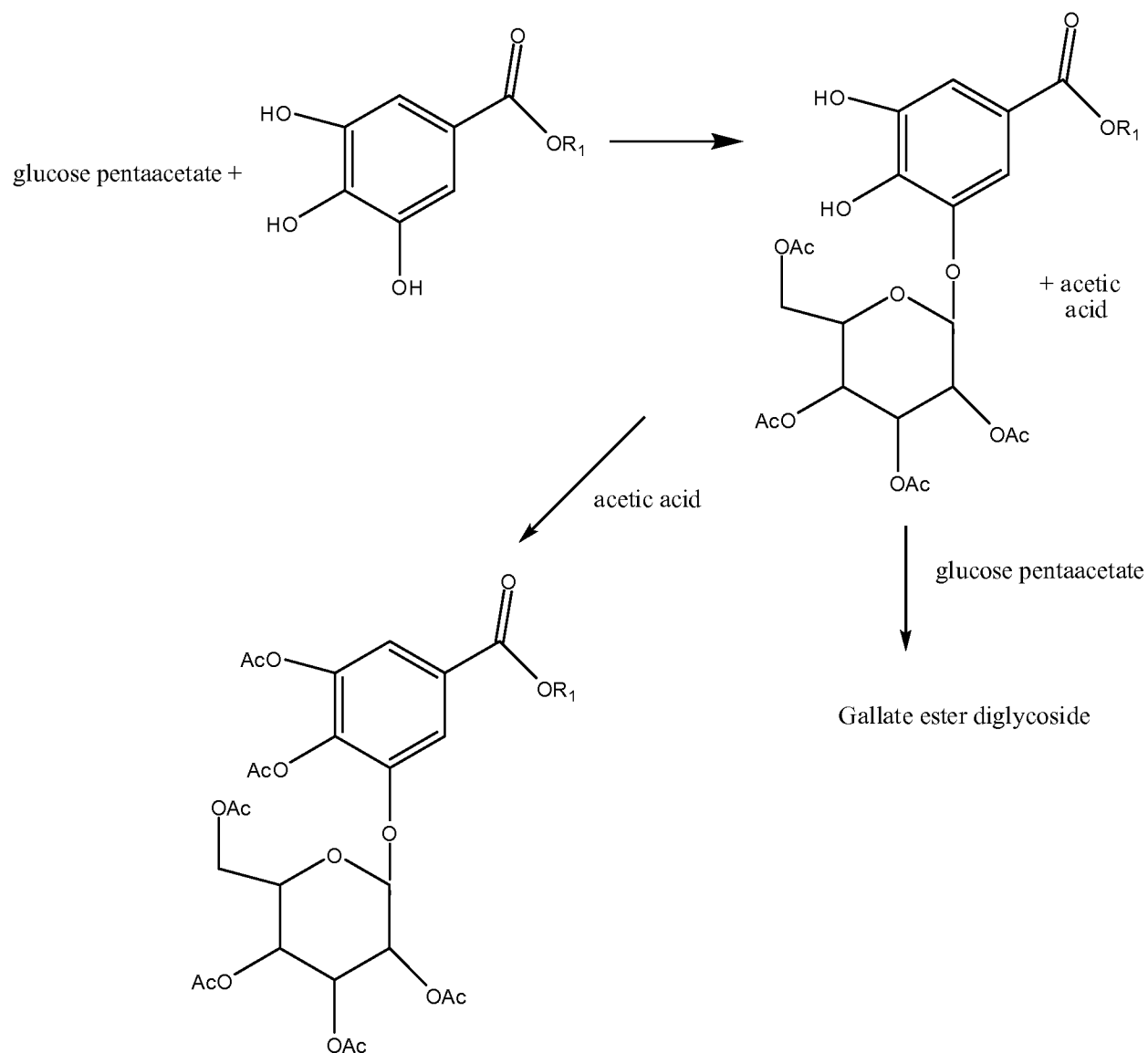
Applicants have traversed the rejection under 35 USC 103 arguing that:

Instant claim 1 has been amended to recite a specific rate at which the acetic acid and solvent are removed from the reaction system via distillation relative to a mole of the alkyl gallate and also the substrate concentration. The method recited in the instant claims provide unexpected results. The prior art taken alone or in combination do not teach or suggest the subject matter of the claimed invention.

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Applicants' arguments and the amendments as recited in instant claim 1 have been considered but they are not found to be persuasive.

The reactions taking place in the instant method is depicted below:



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First of all, the product as instantly claimed is made by reacting gallic acid methyl ester with glucose pentaacetate. The first step in this reaction is the formation of the monoglycoside of gallic acid methyl ester and acetic acid (by-product). Now, in order to form the diglycoside, the monoglycoside of gallic acid methyl ester should react with a second mole of glucosepentaacetate. This second step will also generate acetic acid as a by product. Since gallic acid methyl ester moiety in the monoglycoside product has two unreacted OH groups, these OH groups can react with the acetic acid generated to form the acylated monoglycoside (shown at the bottom left in the reaction scheme above). This would be a competing side reaction (leading to an unwanted product) in addition to the reaction of the second mole of glucosepentaacetate to form the diglycoside (desired product). The reaction of acetic acid with the OH group of the gallic acid methyl ester moiety of the monoglycoside to give the unwanted by-product is an esterification reaction (reaction between acetic acid and an alcohol). This is a fundamental reaction in organic chemistry as taught by March et al above and also well known to one of ordinary skill in the art. In order to prevent this unwanted side reaction from taking place in the system the skilled artisan knows that the acetic acid that is generated in the system should be removed as and when it is formed. One of skill in the art will also recognize that the acetic acid formed can also react with the gallate ester (starting material) and prevent the formation of the monoglycoside of the gallate ester. This would be a second competing reaction, both of which will lower the yield of the desired diglycoside. The removal of acetic acid under reduced pressure is taught in the prior art of record in an analogous reaction (Toshiyuki, page 3, paragraph 9). So, one of ordinary skill in the art would want to remove the acetic acid and solvent and keep concentration of acetic acid below 1.0 % or even less in order to suppress the

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unwanted reaction of the monoglycoside with the acetic acid since this prevents the addition of a second glucose unit to the gallic acid part to form the desired diglycoside. The prior art may not have taught the rate at which the acetic acid is to be removed from the system nor the substrate concentration. These two are process parameters that one of ordinary skill in the art will adjust in order to optimize the yield of the desired product. Therefore, applicants' assertion that they have discovered that the removal of acetic acid at the rate as instantly claimed results in a high yield of the target compound, is not an unexpected result. It is an optimization of the process parameters. It is a well known and expected result based on the type of reaction taking place. This is also well known to one of ordinary skill in the art and the artisan will recognize all of this from the teaching of the prior art and based on his or her own general knowledge and will adjust parameters as instantly recited in order to maximize the yield of the desired product. Toshiyuki may not teach the formation of a diglycoside compound. But the skilled artisan knows that his teaching can be extended to the preparation of the diglycoside compound as instantly claimed since the chemistry is the same and requires the use of an excess of the glucose pentaacetate to react with the monoglycoside in a second step to form the desired diglycoside. There is a suggestion in the prior art that the instant method can be used to make the product of instant formula (3) with a reasonable expectation of success.

Conclusion

Claims 1 and 21-23 are rejected

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THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ganapathy Krishnan/

Examiner, Art Unit 1623

/Shaojia Anna Jiang/

Supervisory Patent Examiner, Art Unit 1623